

AMENDMENT

✓ Following the abstract, please insert the attached Sequence Listing with subsequent page numbering thereafter.

Please amend the specification as follows:

Please enter the following replacement paragraph at page 6, line 13, to page 7, line 2:

DI FIG. 1 is a schematic diagram illustrating a genetic system for monitoring caspase activity in yeast using a transcriptional reporter. Yeast were created that express a chimeric type-1 transmembrane protein (CLBDG6) in which the N-terminal signal sequence and transmembrane domain (CD4) is followed by a linker consisting of 6 tetrapeptide caspase target sites (indicated in bold) that bracket the specificity of known caspases and granzyme B (Thornberry, N. A., *et al.*, *J. Biol. Chem.* 272: 17907-17911, 1997)-**DEV**DG-**WEH**DG-**IEH**DG-**IET**DG-**DEH**DG-**DQM**DG -(SEQ ID NO:4) each of which is followed by a glycine residue, which acts as a stabilizing residue in the N-end rule degradation pathway in yeast (reviewed in Varshavsky, A., *Proc. Natl. Acad. Sci. USA* 93: 12142-12149, 1996). C-terminal to the caspase target site linker is a transcription factor domain, LexA-B42. The LexA-dependent transcriptional reporter consists of LexA binding sites (LexA UAS) and a promoter (P) upstream of the bacterial *lacZ* gene (*lacZ*) (FIG. 1A). The cells in FIG. 1A act as caspase activity reporters since expression of an active caspase results in CLBDG6 cleavage at the caspase target sites, releasing LexA-B42, which enters the nucleus and activates *lacZ* transcription (see FIG. 1B). A version of CLBDG6 in which the PI aspartates are changed to glycines (CLBGG6) cannot be cleaved by caspases. Cells expressing CLBGG6 act as false positive reporters for molecules that activate *lacZ* expression independent of cleavage at caspase target site (FIG. 1C). As shown in FIG. 1D, if the cells in shown in FIG. 1B express a caspase inhibitor as well as an active caspase, caspase activity, and thus caspase-dependent release of LexA-B42, is inhibited. β -gal levels are decreased compared to cells that express the caspase alone.

Please enter the following replacement table (Table 1) at page 13, lines 1-13:

Table 1
Characteristics of the Caspase Family

Group	Caspase	Synonym	S4-S1 recognition sequence (4 amino acids)	Substrate
<i>Group 1</i>	caspase-1	ICE	WEHD (SEQ ID NO:6), YVAD (SEQ ID NO:7)	Pro-IL1B, pro- caspases-1, -3, 14
	caspase-4	ICErel-II, TX, ICH-2	(W/L)EHD (SEQ ID NO:8)	Pro-IL1B, pro- caspase-1
	caspase-5	ICErel-II, TY	(W/L)EHD (SEQ ID NO:8)	unknown
<i>Group 2</i>	caspase-3	CPP32, Yama, apopain	DEVD (SEQ ID NO:9)	PARP, DFF, SREBP, rho-GD1, pro-caspase-6, -9
	caspase-2	ICH-1		PARP
	caspase-7	Mch3, ICE- LAP3, CMH-1	DEVD (SEQ ID NO:9)	PARP, pro-caspase- 6
<i>Group 3</i>	caspase-6	Mch2	VEID (SEQ ID NO:10)	Lamins A, B1/B2, C, PARP
	caspase-8	FLICE, MAC, Mch5	LETD (SEQ ID NO:11)	PARP
	caspase-9	ICE-LAP6, Mch6	LEHD (SEQ ID NO:12)	PARP
	caspase-10	Mch4		Procaspases-3, -7

In re Application of:
Hay and Hawkins
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Please enter the following replacement paragraph at page 14, line 25, to page 15,
line 4:

D3
The localization sequence can be a nuclear localization sequence, an endoplasmic reticulum localization sequence, a peroxisome localization sequence, a mitochondrial localization sequence, or a localized protein. Localization sequences can be targeting sequences which are described, for example, in "Protein Targeting," Chapter 35, of Stryer, L., Biochemistry, 4th ed., W. H. Freeman, 1995. The localization sequence can also be a localized protein. Some important localization sequences include those targeting the nucleus (KKKRK) (SEQ ID NO: 2), mitochondrion (amino terminal MLRTSSLFTRRVQPSLFRNILRLQST-) (SEQ ID NO: 3), endoplasmic reticulum (KDEL (SEQ ID NO:5) at C-terminus, assuming a signal sequence present at N-terminus), peroxisome (SKF at C-terminus), prenylation or insertion into plasma membrane (CaaX, CC, CXC, or CCXX at C-terminus), cytoplasmic side of plasma membrane (fusion to SNAP-25), or the Golgi apparatus (fusion to furin).

Please enter the following replacement paragraph at page 33, lines 10-16:

D4
The DIAP1 coding region was amplified by PCR using primers that generated an N-terminal myc epitope (EQKLISEEDL) (SEQ ID NO: 1) and introduced into the GST expression vector pGEX4T-1 (Pharmacia). The GST-myc-DIAP1 fusion protein was expressed in *E. coli* strain BL21(DE3)pLysS (Novagen) and affinity purified on glutathione-Sepharose by standard methods. The eluted protein was dialyzed against buffer A [25 mM Tris (pH 8.0), 50 mM NaCl, 10 mM DTT]. Following dialysis, the protein was frozen in aliquots after addition of glycerol to 10 %.